all require determining or detecting the presence or absence of IgA anti-Ompc antibodies.

Regarding the Withdrawn Claims

As noted above, claims 1 to 13 are pending in the present application. Claims 8 to 13 were withdrawn from examination as the result of a restriction requirement. As discussed in the telephone interview, while claim 8 and independent claim 10 each recite determining the presence or absence of other antibodies, they each also require determining the presence or absence of IgA anti-OmpC antibodies. For this reason, claims 8 to 11 should therefore be examined together with claims 1 to 7. Applicants appreciate the Examiner's reconsideration of the restriction requirement and respectfully request that claims 8 to 11 be rejoined with the subject matter presently under examination.

Regarding the amendment

Claim 2 has been amended to indicate that determining the presence or absence of IgA anti-OmpC antibodies occurs through detection of a labeled complex containing OmpC antigen or a reactive fragment thereof and IgA antibody to the OmpC antigen. The amendment is supported throughout the specification, for example, at page 8, lines 5-7, which indicates that IgA anti-OmpC

antibodies can be detected with an enzyme-linked immunosorbent assay, and in Example II (pages 32-33), which describes complexes formed by incubation of OmpC antigen with alkaline phosphatase conjugated anti-human IgA indicator antibody.

As set forth above, the amendment is supported by the specification as originally filed and does not add new matter. Furthermore, the amendment is within the scope of the subject matter previously examined and, therefore, does not raise new issues for consideration and does not require a new search. The amendment was not made earlier in prosecution because Applicants maintain that the claim was definite as written. Further, the amendment places the application in better condition for allowance or appeal. For these reasons, Applicants respectfully request entry of the amendment.

Attached hereto as Appendix A is a marked up version of the amended claim showing specific text changes made in the enclosed amendment using underlining to indicate text added.

Regarding the rejection of claims 2 to 7 under 35 U.S.C. § 112, second paragraph

The rejection of claims 2 to 7 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite is respectfully traversed.

In maintaining the rejection, the Office asserts that the use of a label is an essential element not recited in independent claim 2. In regard to Applicants' previous arguments, the Office Action opines that use of an enzyme-linked secondary antibody exemplifies detection using an enzyme as a label. The Office Action therefore concludes that it is not clear how determining the presence of IgA anti-OmpC antibodies can be performed without the presence of some type of label.

Applicants submit that claim 2 is clear and definite to the skilled person as written. However, to advance prosecution, claim 2 has been amended to recite detection of a labeled complex that contains OmpC antigen or a reactive fragment thereof and IgA antibody to the OmpC antigen. Applicants therefore respectfully request reconsideration and withdrawal of this rejection.

Regarding the rejection of claims 1 to 4 under 35 U.S.C. § 102(e) over Braun et al.

The rejection of claims 1 to 4 under 35 U.S.C. § 102(e), as allegedly anticipated by U.S. Patent No. 6,033,864 to Braun et al., is respectfully traversed.

The Office maintains that the Braun et al. patent describes diagnosis of Crohn's disease in a subject using an OmpC antigen, relying on two passages in the cited patent to support the rejection. The first passage at column 11, lines 16-67, describes diagnosing ulcerative colitis in a subject suspected of

having inflammatory bowel disease. The second passage at column 6, lines 36-41, defines a subject suspected of having inflammatory bowel disease as any animal capable of having ulcerative colitis that exhibits one or more symptoms of ulcerative colitis or Crohn's disease. It is asserted that these passages put one skilled in the art in possession of the claimed invention.

Applicants submit that neither of the specific passages cited nor Braun et al. as a whole describes diagnosis of Crohn's disease. Rather, Braun et al. describe diagnosis of ulcerative colitis in a subject suspected of having inflammatory bowel disease, i.e., suspected of having either ulcerative colitis or Crohn's disease.

As noted in the Office Action, a subject suspected of having inflammatory bowel disease is one having a symptom of ulcerative colitis or Crohn's disease. However, having one or more symptoms of Crohn's disease is not synonymous with a diagnosis of Crohn's disease. In this regard, Applicants would point out that inflammatory bowel disorders, such as ulcerative colitis and Crohn's disease, have overlapping clinical and pathologic symptoms, see, for example Merck Manual, 16th ed., pp. 830-839 (1992), attached hereto as Exhibit 1. Therefore, diagnosis of Crohn's disease or ulcerative colitis cannot be based solely upon a subject's symptoms.

In sum, in contrast to the claimed invention, the Braun et al. patent is directed to diagnosis of ulcerative colitis. Nothing in Braun et al. teaches diagnosis of Crohn's disease, as required in the claimed invention. Thus, the Braun et al. patent cannot anticipate the present invention, and Applicants therefore respectfully request reconsideration and removal of the rejection of claims 1 to 4 under 35 U.S.C. § 102(e) over Braun et al.

Regarding the rejection of claims 5 to 7 under 35 U.S.C. § 103 over Braun et al. in view of Targan et al.

Claims 5 to 7 stand rejected under 35 U.S.C. § 103(a), as allegedly obvious over U.S. Patent No. 6,033,864 to Braun et al., in view of U.S. Patent No. 5,932,429 to Targan et al. The rejection has been maintained, in part, because the Braun et al. patent allegedly describes diagnosis of Crohn's disease by determining the presence of IgA anti-OmpC antibodies and the Targan et al. patent allegedly describes diagnosis of Crohn's disease by determining the presence of ASCA.

Claims 5 to 7 depend from independent claim 2 and include the steps of determining the presence or absence of IgA anti-OmpC antibodies in the subject and further determining the presence or absence of IgA anti-*Saccharomyces cerevisiae* antibodies (ASCA) in the subject. The presence of IgA anti-OmpC antibodies or the presence of IgA ASCA in the subject indpendently indicates that the subject has Crohn's disease.

Applicants respectfully traverse the rejection because the combination of references does not teach or suggest diagnosis of Crohn's disease by determining the presence of IgA anti-OmpC antibodies. Firstly, the combination of references does not describe diagnosis of Crohn's disease by the claimed method. The claimed method recites contacting a sample with OmpC antigen or a reactive fragment thereof under conditions suitable to form a complex of the antigen and an IgA anti-OmpC antibody and contacting the complex with anti-IgA antibody. Determining the presence of IgA anti-OmpC antibodies indicates that the subject has Crohn's disease. As discussed above with regard to the rejection under 102(e), Braun et al. do not describe diagnosis of Crohn's disease. Furthermore, neither Targan et al. alone, nor together with Braun et al., teaches or suggests diagnosis of Crohn's disease by detecting the presence of IgA anti-OmpC antibodies.

In particular, as discussed in Applicants' response filed December 13, 2001, Targan et al. do not describe contacting a sample with an OmpC antigen, a microbial antigen, to detect the presence or absence of IgA anti-OmpC antibodies. Rather, Targan et al. describe detecting the presence or absence of perinuclear anti-neutrophil cytoplasmic antibody (pANCA), which is by definition a "neutrophil" antigen (column 7, lines 17-21) that is distinct from OmpC antigens. Given that Braun et al. relates to diagnosis of ulcerative colitis and that Targan et al. relates to the use of an antigen distinct from the OmpC antigen, the combination of Braun et al. and Targan et al. does not describe

diagnosis of Crohn's disease in a subject by detecting the presence or absence of IgA anti-OmpC antibodies.

In sum, for the combination of references to render the claimed invention obvious, each feature of the claimed invention must be described or suggested by the combination. In the instant case, the combination of references does not teach or suggest diagnosis of Crohn's disease by determining the presence or absence of IgA anti-OmpC antibodies. Accordingly, Applicants request reconsideration and removal of the rejection of claims 5 to 7 under 35 U.S.C. § 103(a) over Braun et al. in view of Targan et al.

CONCLUSION

In light of the amendments and remarks herein, Applicants submit that claims 1 to 11 are now in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, she is invited to call the undersigned agent or Cathryn Campbell.

Respectfully submitted,

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APPENDIX A

Amendment to claim:

2. (Twice Amended) A method of diagnosing Crohn's disease in a subject, comprising the steps of:

(a) obtaining a sample from a subject suspected of having inflammatory bowel disease;

(b) contacting the sample with an OmpC antigen, or reactive fragment thereof, under conditions suitable to form a complex of the OmpC antigen, or reactive fragment thereof, and IgA antibody to the OmpC antigen;

(c) contacting said complex with an anti-IgA antibody **to form a labeled complex**; and

(d) detecting **said labeled complex, thereby determining** the presence or absence of IgA anti-OmpC antibodies,

where the presence of said IgA anti-OmpC antibodies in said subject indicates that said subject has Crohn's disease.